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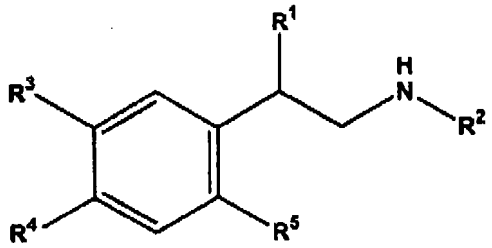
Serial no.: 10/512,024



1. (Previously Presented) A multifunctional β-agonist compound being ROS scavenger and NO donor of Formula 1:




or its salt, wherein $R^1$ is —SNO;

$R^2$ is ROS scavenger group or a NO donor group connected to the —NH group via a linker made of $C_5$-$C_8$ cyclic alkyl, or straight or branched $C_1$-$C_{15}$ alkyl in which one carbon atom is optionally replaced by oxygen or nitrogen, wherein said ROS scavenger group is selected from a nitroxide free radical, alkenyl, sulfhydryl or dithiol moiety in oxidized or reduced form, and aryl, and wherein said NO donor group is selected from —ONO, —$ONO_2$, —SNO, and —NONOate or $R^2$ is $C_5$-$C_8$ cyclic alkyl, or straight or branched $C_1$-$C_{15}$ alkyl;

$R^3$ and $R^4$ together form a substituted 5 to 7-membered saturated heterocycle having 1 or 2 heteroatoms independently selected from nitrogen, and oxygen, and sulfur;

$R^5$ is selected from the group consisting of —H and straight or branched chain $C_1$-$C_{15}$ alkyl;

and whereas any of said alkyl groups is optionally substituted with one or more functional groups selected from hydroxyl, bromo, fluoro, chloro, iodo, mercapto or thio, cyano, alkylthio, aryl, carboxyl, carbalkoyl, alkenyl, nitro, amino, alkoxyl, amido;

wherein at least one of $R^1$, $R^2$, $R^3$ and $R^4$ comprises at least one ROS scavenger selected from the group of moieties consisting of a nitroxide free radical, alkenyl, sulfhydryl or dithiol in oxidized or reduced form, and aryl; and

wherein one or more of $R^1$, $R^2$, $R^3$ and $R^4$ comprise at least one NO donor selected from —ONO, —$ONO_2$, and —SNO.

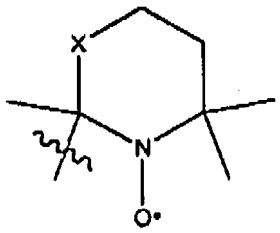
2. (Original) A β-agonist compound according to claim 1, wherein said saturated heterocycle is selected from the group consisting of pyrrolidine, oxazolidine, thiazolidine, tetrahydro 1,3-oxazine, 1,3-dioxane, piperidine, 3-thiapiperidine, and 1,3-thiazine.

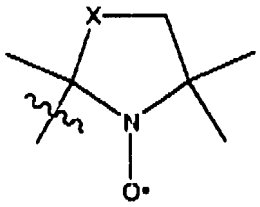
3. (Previously Presented) A β-agonist compound according to claim 2, wherein said saturated heterocycle comprises a substituted nitroxide free radical.

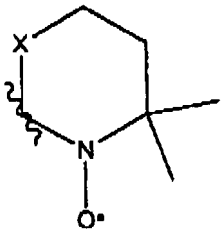
4. (Previously Presented) A β-agonist compound according to claim 3, wherein the nitroxide free radical is a heterocyclyl moiety having the nitrogen atom within a 5-, 6- or 7-membered ring which optionally contains another heteroatom selected from oxygen and sulfur at position beta to the nitrogen, and which is substituted with methyl or ethyl at positions alpha to the nitrogen.

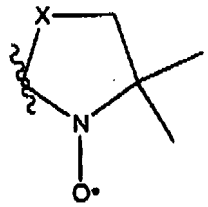
5. (Original) The β-agonist compound of claim 4, wherein said heterocyclyl moiety is linked to the β-agonist moiety via sharing of 1 to 2 atoms, or via a linker.

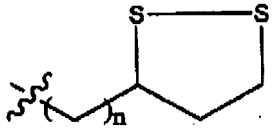
6. (Original) A β-agonist compound according to claim 1, wherein said ROS scavenger group is selected from the group consisting of the following moieties:



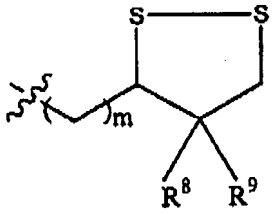



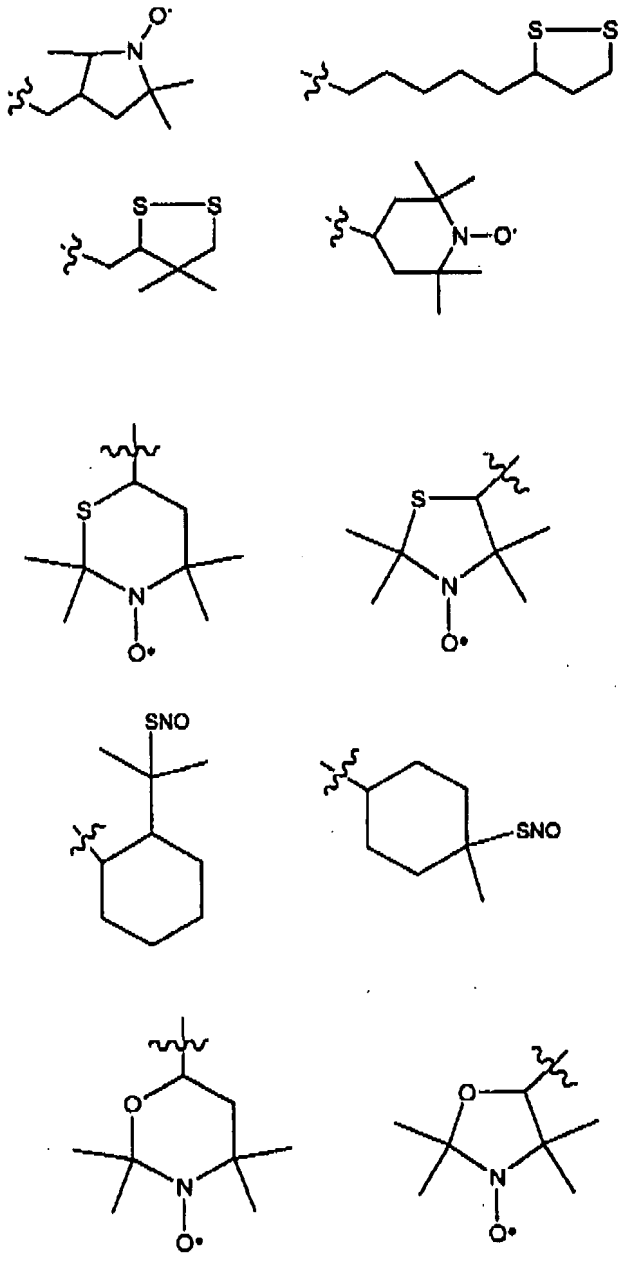




wherein X is selected from carbon, oxygen, and sulfur, and n is an integer from 1 to 15.

7. (Original) A β-agonist compound according to claim 1, wherein $R^2$ is selected from the following structures:

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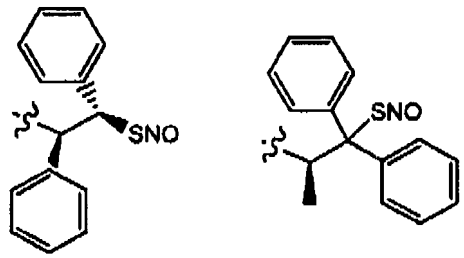
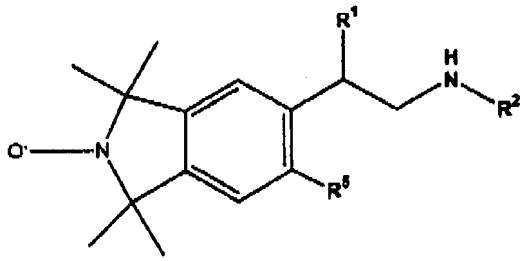



wherein m is 1-6 and $R^8$ and $R^9$ are independently $C_1$-$C_3$ alkyl or —H.

8. (Previously Presented) A β-agonist compound having the formula:

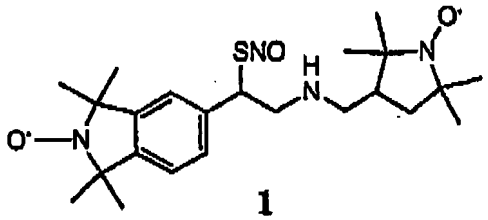



or its salt; wherein $R^1$ is —SNO;

$R^5$ is hydrogen;

and $R^2$ is a moiety selected from a nitroxide free radical having the nitrogen atom within a 5-, 6- or 7-membered saturated ring and which is substituted by up to four methyl groups at positions alpha to the nitrogen, sulfhydryl or dithiol moiety in oxidized or reduced form, —ONO, —$ONO_2$, and —SNO, wherein said moiety is connected to the —NH group directly or via a linker made of $C_1$-$C_6$ alkyl, and which linker is optionally substituted by one or more phenyl groups.

9. (Previously Presented) A multifunctional β-agonist compound according to claim 1 having one of the following structures:

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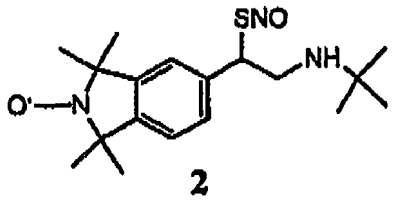


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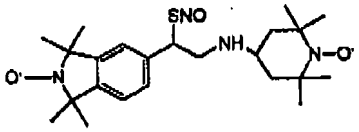


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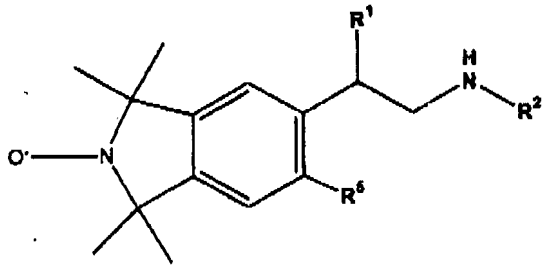
10. (Canceled)

11. (Canceled)

12. (Previously Presented) A process of preparing an agonist according to claim 1 being a compound of the formula:




or its salt, wherein $R^1$ is —SNO;

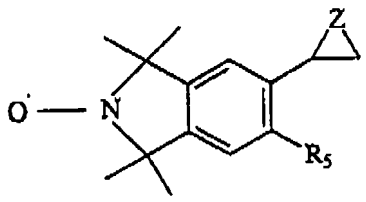
$R^2$ is ROS scavenger group or a NO donor group connected to the —NH group via a linker made of $C_5$-$C_8$ cyclic alkyl, or straight or branched $C_1$-$C_{15}$ alkyl, wherein said

ROS scavenger group is selected from a nitroxide free radical, alkenyl, sulfhydryl or dithiol moiety in oxidized or reduced form, and aryl, and wherein said NO donor group is selected from —ONO, —$ONO_2$, and —SNO or $R^2$ is $C_5$-$C_8$ cyclic alkyl, or straight or branched $C_1$-$C_{15}$ alkyl;

and $R^5$ is selected from the group consisting of —H and straight or branched chain $C_1$-$C_{15}$ alkyl;

and whereas any of said alkyl groups is optionally substituted with one or more functional groups selected from hydroxyl, mercapto, aryl, alkenyl, nitro, and alkoxyl;

which process comprises reacting a chiral or non-chiral epoxide or thioepoxide of the formula




with an amine of the formula $H_2N$—$R^2$

wherein Z is oxygen or sulfur;

$R^2$ is a $C_5$-$C_8$ cyclic alkyl, or straight or branched $C_1$-$C_{15}$ alkyl linked to a group selected from a nitroxide free radical, alkenyl, sulfhydryl or dithiol moiety in oxidized or reduced form, aryl, —ONO, —$ONO_2$, and —SNO; wherein said alkyl is optionally substituted with one or more functional groups selected from hydroxyl, mercapto, aryl, alkenyl, nitro, alkoxyl, $C_1$-$C_5$ alkyl, $C_1$-$C_5$ alkoxy, phenyl, and —$CH_2OH$;

and $R^5$ is selected from the group consisting of —H and straight or branched chain $C_1$-$C_{15}$ alkyl.

13. (Original) A process according to claim 12, wherein said epoxide is prepared from N-benzylphthalimide.

14. (Previously Presented) A process according to claim 12, further comprising converting —SH groups to —SNO groups in the presence of HCl and $NaNO_2$.

15. (Original) A composition comprising a multifunctional β-agonist compound of claim 1, or a salt thereof or a solvate thereof or an optical isomer thereof, for use as a medicament.

16. (Original) A method of treating or preventing a respiratory disorder in a mammal in need thereof comprising administering to said mammal an effective amount of a multifunctional β-agonist compound of any one of claims 1 to 9, or a salt thereof or a solvate thereof or an optical isomer thereof.

17. (Original) A method according to claim 16, wherein said disorder is selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, emphysema, chronic obstructive pulmonary disease, chronic obstructive airway disease, acute respiratory distress syndrome (ARDS) or severe acute respiratory syndrome (SARS) in child or adult, pneumonia, pneumonitis, and restrictive diseases of the lungs.

18. (Original) A method according to claim 16, comprising symptoms selected from the group consisting of recurrent obstruction to air flow within the lung, increased resistance to air flow, narrowing or restriction of an airway, inflammation, bronchial hyperreactivity, airway hyperresponsiveness, mucosal edema, mucus plugging and hypersecretion, and reduced expansion of respiratory parenchyma.

19. (Original) A method according to claim 17, wherein said asthma is selected from the group consisting of atopic, extrinsic, and intrinsic.

20. (Original) A method according to claim 16, wherein said administration is selected from the group consisting of systemic administration and topical administration.

21. (Original) A method according to claim 16, wherein said β-agonist compound is administered by a route selected from the group consisting of oral, parenteral, intramuscular, intraperitoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, implant, buccal, inhalation spray, nasal, vaginal, rectal, and sublingual route.

22. (Original) A method of claim 16, wherein said mammal is human.

23. (Original) A pharmaceutical composition comprising a β-agonist compound of any one of claims 1 to 9, or a salt thereof or a solvate thereof or an optical isomer thereof.

24. (Original) A pharmaceutical composition according to claim 23, further comprising carriers, adjuvants, and excipients.

25. (Original) A pharmaceutical composition according to claim 23, further comprising an active agent selected from the group consisting of mucolytic, bronchodilator, muscle relaxant, decongestant, respiratory stimulant, vasodilator, β-agonist, antiallergic, antiasthmatics, analgesic, anti-inflammatory, antibiotic, antifungal, antiprotozoal, and antiviral agent.

26. (Original) A method according to claim 21, wherein said administration is via an inhalation device.

27. (Previously Presented) An inhalation device for administering a multifunctional β-agonist compound or its salt according to claim 1.

28. (Previously Presented) A kit comprising an inhalation device according to claim 27, in which said multifunctional β-agonist is in the form of fine power or solution or suspension, wherein said powder or solution or suspension optionally contains other components selected from bulking agent, buffer, carrier, excipient, additive, antioxidant, stabilizer, surfactant, odorant, and a second pharmaceutically active agent.